3

MOLECULAR BIOLOGY AND PHARMACOLOGY OF NPY/PYY/PP RECEPTORS: HOW MANY MORE SUBTYPES? C. Gerald, M.W. Walker, K.E. Smith, P.J.-J. Vaysse, T.A. Branchek and R.L. Weinshank. Synaptic Pharmaceutical Corporation, 215 College Road, Paramus, NJ 07652-1431 USA.

Through activation of membrane bound receptors, neuropeptide Y (NPY) and related peptides participate in a diverse range of important physiological activities such as memory, pain, blood pressure, appetite, anxiety and circadian rhythm. Previous functional and binding data support the existence of multiple receptor subtypes including Y1, Y2, Y3, Y4 (PP), "atypical" Y1 and PYY preferring. To date, the rat, human and various other species homologs of the Y1, Y2 and Y4 receptor subtype cDNAs have been cloned and characterized. Protein sequence analysis reveals that the Y1, Y2 and Y4 receptors are members of the G protein-coupled superfamily. When compared to the Y1 subtype, the Y2 and Y4 receptors display an overall amino acid identity of only 31% and 42%, respectively (41% and 55% in the seven membrane spanning regions). Northern blot analysis reveals a broad distribution of the Y1 and Y2 mRNAs in human brain. Southern blot analysis is consistent with the human genome containing a single gene for each of the Y1, Y2 and Y4 receptors.

All three receptor subtypes have been reported to couple to inhibition of adenylate cyclase and increase in calcium mobilization. In addition, when injected in oocytes, the Y1 receptor has been shown to couple to the G protein-activated K^+ channel Girk1, and the Y2 subtype has been shown to inhibit Ca^{2+} influx through voltage-dependent calcium channels in neuronal cell lines.

Following in vivo feeding studies, the existence of an "atypical" Y1 receptor has been postulated by several groups. Subsequent to functional studies where the rank order of potency of the tested peptides did not fit any previously identified receptor subtype, a putative PYY preferring receptor has been proposed. The molecular biology and pharmacology of a newly isolated NPY receptor subtype will be discussed.

4

NPY-IMMUNOPOSITIVE STRUCTURES OF THE RAT AUTONOMIC GANGLIA DURING POSTNATAL ONTOGENESIS. V.V. Glinkina, L.A. Knyazeva, I.G. Charyeva, A.S. Pylaev. Dept. of Morphology, Russia State Medical University, Ostrovityanova str., 1, 117869, Moscow, Russia.

NPY is widely represented in the peripheral nervous system. Approximately one half of the monoaminergic neurons of sympathetic ganglia in various mammals contains NPY as a cotransmitter. NPY is visualized in nonadrenergic and noncholinergic neurons of the autonomic ganglia as well and can form any combinations with other neuropeptide (VIP, galanin, dinorphin, enkephalines, etc).

Among synaptic effects of NPY it may be noted on the one side inhibition of the noradrenaline release from presynaptic terminales and on the other side potentiation of the array of postsynaptic actions. Postnatal localization and dynamics of the density of NPY structures has not been examined. This study was intended to establish distribution of the NPY-positive structures in autonomic ganglia at various stages of the postnatal ontogenesis.

The following ganglia of the Wistar rats were studied: g. nodosum, lumbar ganglia of sympathetic trunk, main pelvic ganglion and intramural cardiac ganglia. The use of immunohistochemical method permits us to reveal three types of NPY-positive(+) structures: i- NPY+varicosities around the neurones; ii- thin NPY+ varicosities situated irregularly; iii- thick NPY+ fibres with the large number of varicosities. In addition, we found NPY-positive neurones. The pattern of the relationship and distribution of the NPY+ structures was an individual feature of each ganglion and age-dependent. Dynamics of the density of NPY+ structures was identical to all ganglia under study. It was characterized by a low level in newborn rats, marked elevation for first two postnatal weeks, and achievement of the definitive values toward the fourth week. Reduction of the number of the NPY+ structures was found in aged rats.

Source: https://www.industrydocuments.ucsf.edu/docs/thcb0000